Amendment to the Specification

Please replace Sequence Listing pages 57-87 currently on file with the enclosed Sequence Listing pages 57-103.

Please replace the paragraph beginning at page 4, line 23, with the following amended paragraph:

--Figure 1 is a schematic diagram representing a method for producing the gene construct of the present invention containing the inducible proline-rich protein (PRP) promoter/enhancer. More specifically, Figure 1 is a schematic diagram illustrating the steps in the construction of the transgenes R15/APPA+intron and R15/APPA used for the generation of transgenic mice. (SEQ ID NO: 36)--

Please replace the paragraph beginning at page 4, line 32, with the following amended paragraph:

--Figure 3 is a schematic diagram representing a method for producing the gene construct of the present invention containing the constitutive parotid secretory protein (PSP) promoter/enhancer. More specifically, Figure 3 is a schematic diagram illustrating the steps in construction of the transgenes Lama2/APPA that codes for the native AppA phytase and the Lama2/PSP/APPA that codes for the AppA phytase with the PSP signal peptide sequence. (SEQ ID NOS: 37 & 38)--

Please replace the paragraph beginning at page 19, line 9, with the following amended paragraph:

--Because a large part of Lama 2 had not been sequenced, the construct was first disassembled and subcloned into pBluescript KS(+) and after incorporation of the *APPA* gene, the Lama 2 was reassembled back (Figure 3). We used unique enzymes Rsrll and Sma1 to remove a 3.4 kbp fragment from Lama2, which was subcloned into

the multiple cloning site (MCS) of pBluescript II KS(+) that was previously digested with Kpn1 and Sma1, using a Kpn1-RsrII adapter (Figure 3, step 1).

      Kpnl*   RsrII

        TGGGAGGTCG <u>(SEQ ID NO: 8)</u>

    CATGACCCTCCAGCCAG <u>(SEQ ID NO: 9)</u>--

Please replace the paragraph beginning at page 19, line 18, with the following amended paragraph:

--That allowed us to preserve the RsrII (CG/GWCCG) <u>(SEQ ID NO: 10)</u> site and destroy the Kpn1 site (GGTAC/C <u>(SEQ ID NO: 11)</u>> GGTAC/<u>T</u> <u>(SEQ ID NO: 12))</u>, which would otherwise interfere with future cloning. The pKS/Lama construct was digested with Apa1 and Kpn1 and used in a three-way ligation with the modified APPA (Figure 3, step 2). We designed two PSP/APPA constructs. One construct APPA-signal/APPA (Figure 3, steps 3a-7a) had the original bacterial signal sequence from the APPA protein having the following amino acid sequence:

Met-Lys-Ala-Ile-Leu-Ile-Pro-Phe-Leu-Ser-Leu-Leu-Ile-Pro-Leu-Thr-Pro-Gln-Ser-Ala-Phe-Ala <u>(SEQ ID NO: 13)</u>--

Please replace the paragraph beginning at page 19, line 28, with the following amended paragraph:

--We also modified a sequence near the ATG codon to resemble the optimal mammalian Kozak sequence (GCC GCC A/GCC ATG G) <u>(SEQ ID NO: 14)</u> (Kozak 1987), but we did not mutagenize the +4 position because it would change Lys to Glu in the signal sequence with possible deleterious consequences for protein export. This optimized sequence was used in our previous construct R15/APPA and led to high levels of phytase production. We checked the APPA bacterial signal sequence using the PSORT computer neural network trained on eukaryotic signal sequences and further described at http://psort.nibb.ac.jp:8800/ (Nakai and Kanehisa 1992). The APPA

bacterial signal sequence was recognized as an efficient leader peptide and the cleavage site was correctly predicted. PSORT also predicted that there is a high probability that phytase would be exported correctly outside of the cell. There were also publications showing that some bacterial signal sequences might function efficiently in mammalian cells (Williamson *et al.* 1994) (Hall *et al.* 1990). Our experiments using cell culture demonstrated that the APPA signal was correctly processed with export of phytase outside of the cell.--

Please replace the paragraph beginning at page 20, line 8, with the following amended paragraph:

--Experiments using cell culture cannot predict the direction of export and if phytase were exported into blood vessels instead of salivary ducts that could lead to deleterious effects. That is why we also designed a second construct PSP-signal/APPA (Figure 3, steps 3b-7b) that would preserve the original PSP signal amino acid sequence:

Met-Phe-Gln-Leu-Gly-Ser-Leu-Val-Val-Leu-Cys-Gly-Leu-Leu-Ile-Gly-Asn-Ser-Glu-Ser
(SEQ ID NO: 15).--

Please replace the Table 12 beginning at page 47, with the following amended Table 12:

--Table 12. Primers used for construction and detection of transgenic constructs.

Name	Start-End[1]	Forward/ Reverse	
Primers used in R15/APPA+intron and R15/APPA construction			
APPA-DOWN2		R	TCGGCGCTCACCTTGAGTTC (SEQ ID NO: 16)
APPA-DRA		F	CCGTTTAAAGCCATCTTAATCCCAT (SEQ ID NO: 17)
APPA-SMA		R	GTCCCGGGTATGCGTGCTTCATTC (SEQ ID NO: 18)
CAT-ATG		R	CCATGGTGGCGGCTTTTAGCTTCCTTAGCTCCTGA (SEQ ID NO: 19)
CAT-TAA		F	AGCGCTTGCAGTTTGTAAGGCAGTTATTGGTGCCC (SEQ ID NO: 20)

CAT-UP1		F	TCG AGG AGC TTG GCG AGA TT (SEQ ID NO: 21)
R15-UP1		F	TTTCGGGCCAATGTTGCTGT (SEQ ID NO: 22)
Primers used in SV40/APPA+intron construction			
SV-HIND		F	CCCAAGCTTTACACTTTATGC (SEQ ID NO: 23)
SV-XHO		R	GCCCTCGAGCCTCCTCACTACTTCT (SEQ ID NO: 24)
Primers used in Lama2/APPA and Lama2/PSP/APPA construction			
APPA-CLA	12635-12657	F	GGATCGATAAAAGCCGCCACCATGAA (SEQ ID NO: 25)
APPA-DOWN2	13307-13326	R	TCGGCGCTCACCTTGAGTTC (SEQ ID NO: 26)
APPA-DOWN4	12751-12780	R	GCACGCACACCATGACGACTGACAATCACC (SEQ ID NO: 27)
APPA-KPN	13935-13959	R	CGGGTACCTTACAAACTGCAAGCGG (SEQ ID NO: 28)
APPA-MATURE	12719-12738	F	CAGAGTGAGCCGGAGCTGAA (SEQ ID NO: 29)
APPA-UP2	13210-13229	F	CGAACTGGAACGGGTGCTTA (SEQ ID NO: 30)
LAMA-CLA	12615-12639	R	GCATCGATCTTTGGTTCTGACAAATGG (SEQ ID NO: 31)
LAMA-SIGNAL		R	TGACTCTGAGTTCCCAATGA (SEQ ID NO: 32)
LAMA-UP	12111-12130	F	GTGCTGCTCCAAGTTTGGTG (SEQ ID NO: 33)
Primers for detection of the porcine β-globin gene			
PIG-BGF		F	GCAGATTCCCAAACCTTCGCAGAG (SEQ ID NO: 34)
PIG-BGR		R	TCTGCCCAAGTCCTAAATGTGCGT (SEQ ID NO: 35)

1   The location of the primers shown for Lama2/APPA sequence.
The start and stop codons of *APPA* are indicated in bold letters, the optimal initiation sequence

for translation is italicized, and the restriction sites for restriction enzymes are underlined.--